

### REMARKS

Claims 38, 40, 41, 43, 45, 46, 49, and 65-68 are pending and stand rejected under 35 U.S.C. § 101 and 112, first paragraph (written description and enablement).

Claims 38, 40 and 65 have been amended to product-by-process language and have been amended to original form indicating the control elements are derived from a stress-inducible gene. New claim 69 has been added and is directed to an ancestor of the transgenic mouse, as set forth in previous claim 38. Reconsideration of the application in view of the foregoing amendments and following remarks is respectfully requested.

### 35 U.S.C. §101

The Office rejected the claims under 35 U.S.C. §101 as allegedly lacking utility. In particular, the Office states:

It is emphasized that the specification as filed does not describe a specific utility for the claimed transgenic mouse (comprising two or three constructs as recited)

Therefore, the claimed transgenic mouse is not supported by either a specific and/or substantial utility, since no function can be ascribed to the gene. (Office Action page 3).

Applicants traverse the rejection and submit that the Examiner is applying an improper standard for compliance with the utility requirement.

In particular, as the Examiner has indicated, the Guidelines on the utility requirement provide for three basic utility criteria -- specific, substantial and credible. The above statement indicates the Examiner believes that applicants' utility is credible since credibility has not been challenged. However, the Examiner questions whether applicants provide a specific and substantial asserted utility, or a well-established utility. Applicants submit that, although they need only satisfy one of these two alternatives, they have provided both a specific and substantial utility, as well as a well-established utility, for the transgenic mice of the present invention.

The Utility Guidelines require that only one credible utility need be disclosed in the application. If the applicant has asserted that the claimed invention is useful for any particular practical purpose and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility is improper. Applicants have complied with these standards.

In the pending case, the application sets forth a number of specific uses for the present invention. Particularly stated and claimed is a role of the transgenic mice of the invention to

determine an analyte's effect on the two or more stress-inducible control elements in the mice (claim 40), as well as noninvasive methods for detecting a level of expression in response to an analyte (claim 45). It is clear from the foregoing that Applicants have explicitly set forth specific utilities for the transgenic mice of the subject invention. Thus, Applicants dispute the Examiner's assertion that the claimed invention is not supported by a specific asserted utility.

Previously submitted documents, for example Jankowsky et al. (2001), submitted with Dr. West's Declaration, confirm the assertion in Applicants' specification regarding the utility of the claimed transgenic mice. In particular, Jankowsky et al. describe that multiply transgenic mice express both proteins at high levels. Thus, it is clear that, when the two or more stress-inducible promoters are induced, the claimed mice would produce luciferase at high levels and, accordingly, analytes could be readily screened for their effect on stress-inducible genes. Accordingly, Applicants have indeed asserted a specific and substantial utility in the present application.

It appears that the Examiner will not consider a utility for the claimed animals based on the utility of other multiply transgenic animals but rather is requiring an absolute showing that the transgenic mice function as stated. If this were the standard, the concept of "well known" utility would be meaningless. Applicants submit that they have provided both a specific and substantial utility, as well as a well-established utility, for the molecules of the present invention.

Based on the foregoing, applicants respectfully submit that the rejections under 35 U.S.C. §101, for lack of utility, should be withdrawn.

### **35 U.S.C. §112, First Paragraph, Written Description**

Claims 38, 40, 41, 43, 45, 46, 49 and 65-68 were rejected on the grounds that Applicants' specification fails to sufficiently describe the claimed transgenic mice. (Office Action, pages 4-6).

The Examiner acknowledges that the "applicants have described in the specification a method of producing a transgenic mouse ... " (Office Action, page 5). Accordingly, the foregoing amendments indicating how the transgenic mice are produced in the body the claims (*i.e.*, product-by-process claims) obviates this rejection.

### **35 U.S.C. §112, First Paragraph, Enablement**

The Examiner again maintains that undue experimentation would be required in order to practice the invention of claims 38, 40, 41, 43, 45, 46, 49 and 65-68, stating definitely that only

actual production of the claimed transgenic animals would satisfy this requirement (Office Action, page 7):

In summary, since the art of making transgenic animals is highly unpredictable and unless a transgenic mouse has been produced, one can not predict what will be the characteristics of the transgenic mouse comprising a given panel of expression cassettes and therefore, an artisan would not know how to use the claimed transgenic mouse in claimed methods.

For all the reasons of record, the Examiner's rejection remains legally and factually wrong.

Making Transgenic Mice With Multiple Expression Cassettes is Predictable and Routine

Factually, there is nothing unpredictable about making transgenic mice as claimed, let alone highly unpredictable. Transgenic mice expressing light generating proteins, where light expression is driven by a promoter sequence to which the light generating protein-encoding sequences have been made repeatedly and patented, for example, as described in U.S. Patent Nos. 5,650,135; 6,217,847; 6,649,143; 6,632,978; and 6,566,089.

Likewise, "predicting . . . the characteristics of the transgenic mouse" would be routine to the skilled artisan. They would instantaneously know from the specification that the claimed transgenic animals would be characterized by light-generation when administered an analyte that induces one or more of the transgenic stress-inducible control sequences. Simply put, the transgenic mice are characterized by their ability to generate light under specific conditions, and the skilled artisan would know to use them for studying regulation of stress-inducible genes, for example in response to administration of an analyte.

Thus, the allegations that (1) making transgenic mice is highly unpredictable and (2) that characteristics of such mice is unpredictable are unsustainable and completely refuted by the evidence of record.

Meeting the Enablement Requirement Does Not Require Actual Working Examples

This oft-repeated enablement rejection is also contrary to well-settled law. Legally, there is no requirement that an applicant provide working examples or actually make the claimed subject matter. See, MPEP 2164.02. Indeed, as previously noted with regard to transgenic animals, the Board of Patent Appeals and Interferences has made it abundantly clear that there can be no requirement for a disclosure of what the examiner perceives as possible characteristics

of such a [transgenic animal] product. *Ex parte Chen*, 61 USPQ2d at 1028 (BPAI 2002, unpublished).

Even Patent Office Training materials recognize that claims to transgenic animals are fully enabled where “an enabled use for the claimed transgenic mouse is well established.” (See, Training Materials for Examining Patent Applications with Respect to 35 U.S.C. 112, first paragraph -- Enablement, Example I, page I-6, *circa* 1997).

In the case at hand, and as noted above with the unsustainable new utility rejection, an enabled use for transgenic animals comprising expression cassettes encoding a light-generating protein is well established, as evidenced for example by U.S. Patent No. 6,217,847 which shows the generation of a transgenic animal comprising an expression cassette encoding luciferase and use of these animals for the temporal and spatial analysis of transcriptional control.

When the enablement requirement is determined relative to the pending claims, it is clear that the specification enables the skilled artisan to make and use the claimed rodents.


**CONCLUSION**

Applicant respectfully submits that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned at (650) 493-3400.

Respectfully submitted,

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